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Study of the mechanism of permeabilization of lecithin liposomes and rat liver mitochondria by the antimicrobial drug triclosan

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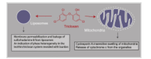
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Highlights

- Triclosan is able to permeabilize the membrane of lecithin liposomes.
- Raising pH of the medium inhibits the triclosan-induced liposome permeabilization
- Laurdan fluorescence data indicate a phase heterogeneity in triclosan/lecithin system
- Triclosan promotes a cyclosporin A-insensitive swelling of rat liver mitochondria.
- Triclosan induces cytochrome *c* release from rat liver mitochondria

Abstract

The effect of the antimicrobial compound triclosan (5-chloro-2′-(2,4-dichlorophenoxy)phenol) on the permeability of lecithin liposomes and rat liver mitochondria was studied. It was found that triclosan was able to increase nonspecific permeability of liposomes in a dose-dependent manner, which was detected by the release of the fluorescent probe sulforhodamine B (SRB) from vesicles. A partial release of SRB occurs instantly at the moment of triclosan addition, which is followed by a slow leakage of the dye. The triclosan-induced release of SRB from liposomes grew as pH of the medium was decreased from 9.5 to 7.5. As revealed by the laurdan generalized polarization (GP) technique, triclosan increased laurdan GP in lecithin liposomes, indicating a decrease in membrane fluidity. Measurements of GP as a function of fluorescence excitation wavelength gave an ascending line for triclosan-containing liposomes, which can be interpreted as phase heterogeneity of the lipid/triclosan system. Dynamic light scattering experiments also showed that at a high triclosan-to-lipid molar ratio (~ 0.5), a population of smaller light-scattering particles (~ 0.4 of the size of liposomes) appear in the system. Experiments with rat liver mitochondria demonstrated that triclosan (10–70 μM) induced a high-amplitude cyclosporin A-insensitive swelling of the organelles accompanied the release of cytochrome *c*. On the basis of the results obtained, possible mechanisms of the toxic effect of triclosan in eukaryotic cells are discussed.





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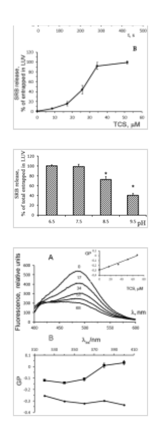
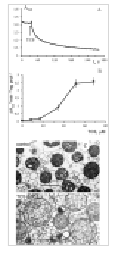
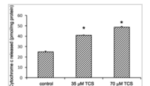
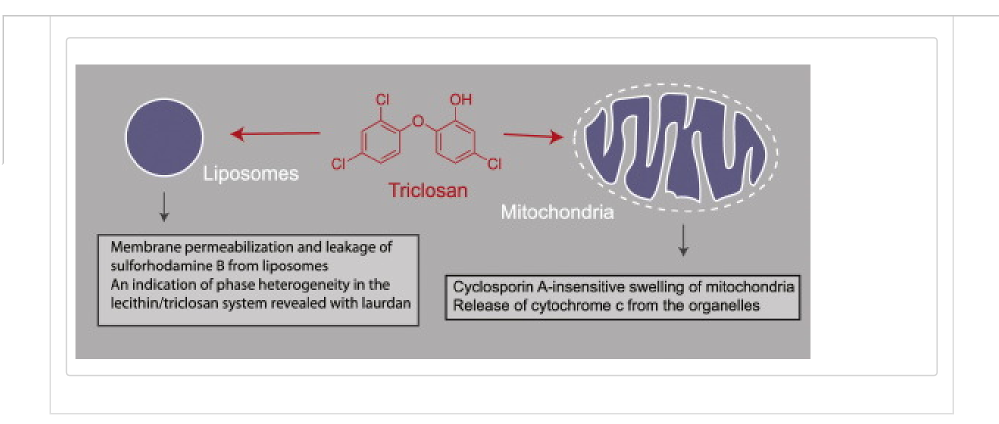


Table 1







Abbreviations

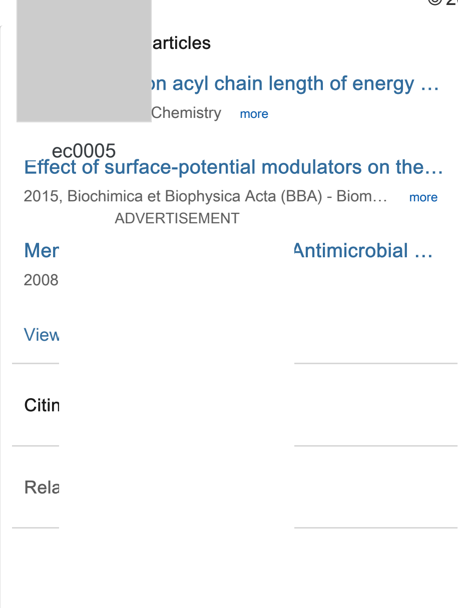
TCS, triclosan; CsA, cyclosporin A; LUV, large unilamellar vesicles; MPT, mitochondrial permeability transition; SRB, sulforhodamine B

Keywords

Triclosan; Membrane permeabilization; Liposomes; Mitochondria



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